REMARKS

Claims 1 through 9 and new Claims 10 and 11 are pending in the application.

Claim 1 has been amended to correct a grammatical error.

Claim 1 has also been amended to emphasize that the inventive processes result in an increased overall yield in comparison to comparable processes incorporating either phosgene or diphosgene. Support for this amendment can be found in the Application-as-filed, for example on Page 2, line 5 through Page 3, line 6.

Claims 10 and 11 have been added to complete the record for examination and highlight advantageous embodiments of the invention.

Claim 10 is directed to advantageous processes in which the chlorocarbonylation reaction is performed with a triphosgene molar ratio of between 0.46:1 and 0.54:1, the base is triethylamine, in a base molar ratio relative to the compound of formula II of between 1.4 : 1 and 1.6 : 1, and the chlorocarbonylation reaction a) is performed in toluene. Support for Claim 10 can be found in the Application-as-filed, for example on Page 4, lines 18 through 22.

Claim 11 is directed to advantageous processes in which the overall yield is about 80 %. Support for Claim 11 can be found in the Application-as-filed, for example on Page 5, lines 16 through 17.

Reexamination and reconsideration of this application, withdrawal of all rejections, and formal notification of the allowability of the pending claims are earnestly solicited in light of the remarks which follow.

35 USC 112 Rejection

Claim 1 stands rejected in that it does not end with a period. Claim 1 has been amended to address the foregoing typographical error. Applicants respectfully request withdrawal of the foregoing rejection.

The Claimed Invention is Patentable in Light of the Art of Record

Claims 1 through 9 stand rejected over HU 63389 ("HU 389") to Haasz et al. in view of Eckert et al. Angewandte Chemie International Edition ("Eckert").

It may be helpful to briefly discuss the invention prior to addressing the merits of the invention.

Oxcarbazepine is a known anticonvulsivant agent. Oxcarbazepine is generally produced by either carbamoylation with cyanates or by chlorocarbonylation followed by ammonolysis and final hydrolysis. An exemplary conventional process by which to form oxcarbazepine via chlorocarbonylation is provided in cited HU 389, discussed in greater detail below. Conventional processes by which to perform the chlororcarbonylation step to date have incorporated either phosgene (per United States Patent No. 3 642 775) or diphosgene (per HU 389).

Unfortunately, the overall yield for oxcarbazepine produced using phosgene in toluene is only about 45 %. The overall yield for oxcarbazepine produced using diphosgene is even lower, with only about a 43 %. In that regard, the Examiner's attention is kindly directed to the Application-as-filed on Page 2, line 5 through Page 3, line 2. Accordingly, a need remains in the art for improved processes by which to form oxcarbazepine.

Altogether unexpectedly, Applicants have found that triphosgene may be used to form oxcarbazepine with greatly improved overall yields in comparison to oxcarbazepine produced using either phosgene or diphosgene. Such a result was unexpected because overall oxcarbazepine yields decrease when diphosgene (containing a mono-chlorinated carbonyl moiety) is substituted for phosgene (containing a di-chlorinated carbonyl moiety). Hence the substitution of triphosgene (containing no carbonyl chloride moiety) for diphosgene (containing a mono-chlorinated carbonyl moiety) would not be expected to increase overall yield. Considered differently, one skilled in the art would expect the reactivity of triphosgene to be even further removed from phosgene than diphosgene, thus a decrease in overall yield would have been expected.

Furthermore, triphosgene is known in the art to present challenges in its use, and thus one skilled in the art would have been further prejudiced against its use. Applicants respectfully direct the Examiner's attention to United States Patent No. 6,340,760 (US 760). US 760 teaches that triphosgene can be limited to laboratory scale production alone; i.e. use of triphosgene leads to a poorer yield than phosgene on an industrial scale. For example, triphosgene can be quite sensitive regarding its solvent, and can thus require an altogether different solvent than used in phosgene reactions. In that regard, the Examiner's attention is kindly directed to United States Patent No. 6,340,760 at Column 3, line 49 through Col. 4, line 8. Consequently, the performance of phosgene within a reaction can not be directly imputed to triphosgene.

Accordingly, the claims as-amended are directed to processes for preparing oxcarbazepine which comprise chlorocarbonylation with triphosgene in the presence of a base, in which the process results in an increased overall yield in comparison to comparable processes incorporating either phosgene or diphosgene.

In particularly advantageous embodiments, the chlorocarbonylation reaction is performed with a triphosgene molar ratio of between 0.46:1 and 0.54:1, the base is triethylamine, in molar ratio of between 1.4 : 1 and 1.6 : 1 and the reaction is performed in toluene, as recited in newly added Claim 10.

In especially expedient aspects, the overall yield of the inventive processes is about 80 %, as recited in newly added Claim 11. Such elevated overall yield is a 78 % improvement over known phosgene-based reactions, and an 85 % improvement over known diphosgene-based reactions.

Applicants respectfully submit that the cited references do not teach or suggest the claimed invention.

HU 389 is directed to use of diphosgene to produce oxcarbazepine. HU 389 discloses an initial yield of 58.9 % and a yield after hydrolysis of 73.5 %, resulting in the overall yield of 43.3 %, as noted within the Application-as-filed on Page 2, line 18 through Page 3, line 2. HU 389 expressly teaches the incorporation of up to a 70 % molar excess of diphosgene.

HU 389, merely teaching the conventional incorporation of diphosgene within oxcarbazepine reactions, thus does not teach or suggest the claimed invention.

HU 389, teaching use of up to a 70% molar excess of diphosgene, further fails to teach or suggest advantageous processes in which the chlorocarbonylation reaction is performed a triphosgene molar ratio of between 0.46:1 and 0.54:1, as recited in Claim 3.

HU 389, silent as to the incorporation of base, likewise fails to teach or suggest advantageous processes in which the base is triethylamine, much less triethylamine in a ratio of between 1.4 : 1 and 1.6 : 1, as recited in Claim 4.

Nor does HU 389 teach or suggest advantageous embodiments in which the chlorocarbonylation reaction is performed with a triphosgene molar ratio of between 0.46:1 and 0.54:1, the base is triethylamine in molar ratio of between 1.4 : 1 and 1.6 : 1 and the reaction is performed in toluene, as recited in newly added Claim 10. HU 389 expressly teaches the incorporation of a molar excess of diphosgene and is silent as to base.

And HU 389, whose overall yield is 43 %, most certainly does not teach or suggest advantageous processes by which to form oxcarbazepine in which the overall yield is about 80 %, as recited in newly added Claim 11.

Eckert does not cure the deficiencies in HU 389.

Eckert generically discloses a number of reactions in which triphosgene may be used. As noted by the Examiner, Eckert notes that triphosgene may be used in chloroformylation reactions. Eckert more particularly indicates that chloroformylation reactions incorporate 1/3: 1 molar ratio triphosgene using pyridine as a nucleophile in a 1:1 molar ratio. (Page 895, first column, second full paragraph and Table 1 "a" and "b"). Eckert recommends triethylamine for other its reactions, however. (Table 1, "c","h" and "i"). Eckert generically teaches that chlorinated solvents, such as dichloromethane or o-dichlorobenzene, are used in conjunction with the triphosgene reactions. (Page 895, second column, lines 1 – 2).

Eckert thus, merely teaching a generic list of triphosgene reactions, thus does not teach or suggest the claimed invention.

Eckert, teaching triphosgene in at a significantly lower molar ratio, further fails to teach or suggest advantageous processes in which the chlorocarbonylation reaction is performed a triphosgene molar ratio of between 0.46:1 and 0.54:1, as recited in Claim 3.

Eckert, teaching pyridine as a nucleophile within chloroformylation reations at a 1:1 molar ratio, likewise fails to teach or suggest advantageous processes in which the base is triethylamine, much less triethylamine in a ratio of between 1.4 : 1 and 1.6 : 1, as recited in Claim 4.

Thus Eckert can not teach or suggest advantageous embodiments in which the chlorocarbonylation reaction is performed with a triphosgene molar ratio of between 0.46:1 and 0.54:1, the base is triethylamine in molar ratio of between 1.4 : 1 and 1.6 : 1 and the reaction is performed in toluene, as recited in newly added Claim 10. Eckert expressly teaches altogether different molar ratios, and further recommends chlorinated solvent for triphosgene reactions.

And Eckert most certainly does not teach or suggest such advantageous processes by which to form oxcarbazepine in which the overall yield is about 80 %, as recited in newly added Claim 11.

Applicants respectfully submit that there would have been no motivation to have combined HU 389 and Eckert. However, even if Applicants had combined HU 389 and Eckert (which Applicants did not do) claimed invention would not have resulted.

The combination particularly does not teach or suggest that processes for preparing oxcarbazepine which include chlorocarbonylation with triphosgene in the presence of a base would result in an increased overall yield in comparison to comparable processes incorporating either phosgene or diphosgene, as recited in Claim 1 as-amended. Applicants particularly respectfully submit that one skilled in the art would not have a reasonable expectation that the method of HU 389 could have been performed with triphosgene in a higher yield. To the contrary, one skilled in the art would instead have expected a lower yield than HU 389, as discussed above. Hence there would have been absolutely no motivation to have substituted triphosgene within the reaction of HU 389.

The combination further fails to teach or suggest advantageous processes in which the chlorocarbonylation reaction is performed a triphosgene molar ratio of between 0.46:1 and 0.54:1, as recited in Claim 3. HU 389 teaches up to a 70 % molar excess diphosgene, while Eckert teaches an altogether different molar ratio.

The combination likewise fails to teach or suggest advantageous processes in which the base is triethylamine, much less triethylamine in a ratio of between 1.4 : 1 and 1.6 : 1, as recited in Claim 4. HU 389 is silent as to the presence of a base, while Eckert teaches pyridine as a nucleophile within chloroformylation reations at a 1:1 molar ratio.

Nor does the combination teach or suggest advantageous embodiments in which the chlorocarbonylation reaction is performed with a triphosgene molar ratio of between 0.46:1 and 0.54:1, the base is triethylamine in molar ratio of between 1.4 : 1 and 1.6 : 1 and the reaction is performed in toluene, as recited in newly added Claim 10. HU 389 expressly teaches the incorporation of up to a 70 % molar excess of diphosgene and is silent as to base. Eckert expressly teaches the incorporation of a significantly lower molar ratio of triphosgene within chloroformylation reactions. Eckert further further expressly teaches pyridine base in a 1:1 molar ratio within a chlorinated solvent.

And the combination most certainly does not teach or suggest such inventive processes for forming oxcarbazepine in which the overall yield of the inventive processes is about 80 %, as recited in newly added Claim 11.

Accordingly, Applicants respectfully submit that HU 389 and Eckert do not teach or suggest the claimed invention, considered either alone or in any combination with the remaining art of record.

CONCLUSION

It is respectfully submitted that Applicants have made a significant and important contribution to the art, which is neither disclosed nor suggested in the art. It is believed that all of pending Claims 1 through 11 are now in condition for immediate allowance. It is requested that the Examiner telephone the undersigned if any questions remain to expedite examination of this application.

It is not believed that extensions of time or fees are required, beyond those which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time and/or fees are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required is hereby authorized to be charged to Deposit Account No. 50-2193.

Respectfully submitted,

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